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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,503	04/23/2001	Edwin J. Iwanowicz	QA231 NP	4455

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EXAMINER
LIU, HONG

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 02/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/840,503	Applicant(s) IWANOWICZ ET AL.	
	Examiner Hong Liu	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *10-23 and 30-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *10-23 and 30-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 10-23 and 30-41 are pending in this application.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 10-23 and 30-41, drawn to the compounds of formula (I) where R1 and R3 or R4 and R5 do not form a ring such that the core is quinolinone, classified in class 546, subclass 312.

II. Claims 10-14 and 30-31, drawn to the compounds of formula (I) where R1 and R3 or R4 and R5 form a ring such that the core is tricyclic, classified in class 546, subclass 79.

The inventions are distinct, each from the other because of the following reasons: Groups I-II are directed to structurally dissimilar compounds such that the variable core created by varying the definitions of the formula do not belong to a recognized class of chemical compounds in the art, and references anticipating one invention would not render obvious the others, for example, a bicyclic hetero ring is different from tricyclic hetero rings. Thus, separate searches in the literature as well as in the U.S. Patent Clarification System would be required. Each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structures as functional equivalents of each other. The mere fact that there is a single similarity is not in itself a significant reason to render the whole embodiment obvious.

2. During a telephone conversation with Ms. Duncan on 01/31/02 a provisional election was made with traverse to prosecute the invention of Group I, claims 10-23 and 30-41. Affirmation of this election must be made by applicant in replying to this Office action.

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicants also elected the species of Example 10. The elected compound was not found in the search and the search was expanded to compounds wherein R1 is alkyl.

Applicants are also advised of MPEP 803.02, Restriction -Markush Claims[R-2], forth paragraph, where is stated;

"As an example, in the case of an application with a Markush -type claims drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the non-elected species would be held withdrawn form further consideration. As in the prevailing practice, **a second action on the rejected claims would be made final.**" (Emphasis added).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Yu et al., Chem Abstract 72: 31563. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 15502-80-4, i.e., R1 is alkyl, R2 is hydroxy.

Claim Rejections - 35 USC § 112

5.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-23 and 15-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for preparation and use of compounds wherein R2 is a monocyclic heteroaryl or cyano, does not reasonably provide enablement for preparation and use of compounds wherein R2 is other than the functional groups specified above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein R2 can be an unsubstituted or substituted, heteroaromatic group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional IMPDH enzyme

inhibitor which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants' claims. Only compounds wherein R2 is oxazole and cyano have been made.

Furthermore, no testing data is provided for the representative compounds, much less all the possible compounds encompassed by the claims. Examples should be of sufficient scope as to justify the scope of the claim. The definitions of the various R2 variables embrace many structurally divergent groups not represented at all in testing, since testing for the instant compounds is not seen in the specification. Markush claims must be provided with support in the disclosure when the "working examples' fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear and exact terms. See In re Fouch, 169 USPQ 429.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonably extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested. In cases directed to chemical compounds which are being used for their physiological activity, the scope of the claims must have a reasonable correlation to the scope of enablement provided by the specification. See In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. No reasonable assurance has been made that the instant compounds as an entire class have the required activities needed to practice the invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability" have been demonstrated to be sufficiently lacking in the instant case for the scope being claimed.

Furthermore, the instant specification provides no direction or guidance for how to use the disclosed (and claimed) compounds since there are no working examples of experimental data to demonstrate that the compounds may inhibit IMPDH. Nor does the specification show that the compounds in combination with phosphodiesterase Type 4 inhibitor may prevent allograft rejection, no teaching how the data provided permits the determination of an effective amount for treating these disorders,. Therefore, in view of the breadth of the claims, the chemical nature of the invention, the unpredictability of in vitro and in vivo correlation, the lack of working examples, and the lack of further guidance in how to use the claimed compounds and compositions to actually treat these disorders, it would require an undue amount of experimentation to use the claimed inventions.

In claims 35and 41, instant claim language embraces disorders not only for treatment but also for PREVENTION which is not remotely enabled. It is presumed in the prevention of disease and/or disorders claimed herein there is a way of identifying those people who may develop allograft rejection. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

7. Claims 10-23 and 30-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of "prodrug" is not adequately enabled. Applicants provide no guidance as how the compounds are made more active in vivo. The choice of a "prodrug" will vary from

drug to drug. Therefore, more than minimal routine experimentation would be required to determine which prodrug will be suitable for the instant invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-15, and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

8. 1). "substituted" alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, etc. throughout claim 1 is unclear as to the nature and number of substituent(s) intended.

2). Claim 36 contains the trademark/trade name of rolipram. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the rolipram derivatives and, accordingly, the identification/description is indefinite.

1. 3). The use of "heterocycloalkyl" in the definition of R is unclear to the array of heteroatoms as well as nature of atoms as ring members. See In re Wiggins 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. The examiner can normally be reached on Monday through Friday from 8:30 AM to 6:00 PM. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for this group is (703) 308-4734 for "unofficial" purposes and the actual number for official business is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose number is (703) 308-1235.

hl
February 4, 2003

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